ATSDR/DRO Activity Form

Preparer's First Name: Lora	Preparer's Last Name: Werner	Preparer's Affiliation: DRO
Site Name: Dimock Residential Groundwater Site		City: Dimock
State/Tribe: PA	Cost Recovery #: 3ATA	EPA ID:	Non-site-specific: ☐
Requester's Name: Dennis Carney, Branch Chief		Phone Number: 215-814-3241
Requester Category	EPA Removal	

Question or Request (full description) | Date of Request (mm/dd/yyyy): 3/12/2012

EPA R3 removal asked ATSDR R3 what concentration of lithium in drinking water would represent an acute public health concern. In addition, ATSDR R3 is interested in establishing whether lithium in the 200-500 ug/L range would represent a public health concern.

Activity (Select all that apply)

- ☐ Chemical Exposure
- ☐ Community Involvement
- ☒ Emergency Response
- ☐ Health Assessment
- ☐ Health Consultation
- ☐ Health Education (Public or Health Care Provider)
- ☐ Outreach Activity
- ☐ Public Meeting
- ☒ Removal
- ☐ Referrals (PEHSU, ACMT)
- ☐ Site Visit
- ☒ Technical Assistance
- ☐ Other (specify)

Special Initiative (Select all that apply)

- ☐ Brownfields
- ☐ CARE Pilot
- ☐ Day care
- ☐ Exercises
- ☐ Land Reuse Sites
- ☐ Mercury response
- ☐ Non-site related (HIA, asbestos, workgroups, etc)
- ☐ School Siting
- ☐ **Success Story**
- ☐ Toxicological data/PDA
- ☐ Training
- ☐ Tribal Activities
- ☐ Other (specify)

ATSDR Response (Detailed description of response) | Date of Response (mm/dd/yyyy): 3/23/2012

EPA R3 removal asked ATSDR R3 what concentration of lithium in drinking water would represent an acute public health concern. In addition, ATSDR R3 is interested in establishing whether lithium in the 200-500 microgram per liter or parts per billion (µg/L or ppb) range would represent a chronic public health concern. ATSDR R3 referred this request to ATSDR Emergency Response. ATSDR ER and the National Center for Environmental Health (NCEH) reviewed information from ATSDR, EPA, FDA, and other available literature on lithium toxicity.

RESPONSE TO QUESTION 1: What concentration of lithium in water would pose an acute human health threat?

Based on the literature reviewed, lithium concentrations in drinking water below 1,500 ug/L would likely not result in adverse acute health effects in children or adults. Based on clinical experience with acute toxicity, 1,500 ug/L represents a conservative level of concern for acute toxicity. There are a few epidemiologic studies associating varying levels of lithium in drinking water with

behavioral effects and effects on thyroid functions. There is a wealth of literature on therapeutic use of lithium and adverse effects over time at doses that are much higher than these environmental exposures.

RESPONSE TO QUESTION 2: Are chronic (1 year or longer) exposures to lithium in drinking water at concentrations in the 200-500 ug/L range a public health concern?

ATSDR cannot determine if chronic consumption to 200-500 ug/L of lithium in drinking water represents a public health concern. ATSDR notes that these levels of ingestion are 1/3 as high as ATSDR's conservative level of concern for acute toxicity. ATSDR also notes that these levels are 10 to 20 fold higher than an EPA provisional reference dose (RfD) for children for chronic /subchronic lithium ingestion. The potential for adverse health effects in sensitive subpopulations is uncertain. There is very little data on lithium exposures in young children. Potentially sensitive populations for lithium exposures include children, pregnant women, and those with significant renal or cardiovascular disease, or dehydration or sodium depletion with concurrent long-term use of medications such as: diuretics (e.g., hydrochlorothiazide), nonsteroidal anti-inflammatory agents (e.g., ibuprofen), calcium channel blocking agents (e.g., verapamil), and angiotensin-converting enzyme inhibitors (e.g., captopril).

RECOMMENDATIONS:

ATSDR cannot predict the health consequences from chronic ingestion of drinking water containing 200 to 500 ug/L because there are not any scientific studies to support this. Individuals using drinking water with these levels of lithium who are sensitive or concerned should consult their personal health care provider and determine if it is prudent to follow their serum lithium levels. ATSDR will provide health education consultation on this issue to impacted residents. ATSDR will also consult with individual healthcare providers, if requested.

ATSDR ACTIVITIES:

ATSDR is in the process of conducting further public health evaluation of the available drinking water data from this site and will make additional conclusions and recommendations about this information as appropriate in a future health consultation document.

BASIS FOR CONCLUSIONS:

Conclusion 1: Lithium salts have been used therapeutically at adult doses varying between 900 mg (mg)/day to 1,800 mg/day to achieve therapeutic serum concentrations ranging from 0.6 to 1.4 millimoles per liter (mmol/L). Concentrations between 0.8 to 1.0 mmol/L are generally accepted as the optimally therapeutic range. A 900 mg dose of lithium carbonate medication contains 170 mg lithium; therefore, 170 mg of lithium for a 70 kg adult equates to roughly 2.5 mg lithium/kg body weight/day. If this is all ingested in 2 liters of water, it would amount to a lithium water concentration of 85,000 ug/L.

Conclusion 2: In general, lithium has a narrow therapeutic-toxic ratio and can induce adverse health effects, if slight changes in dosing or elimination occur. Lithium treatment is not recommended for patients with significant renal or cardiovascular disease, severe debilitation or dehydration or sodium depletion or for patients receiving certain other medications (e.g., diuretics) because the risk of lithium toxicity is very high in such patients. There are several groups of drugs that interact with lithium causing increased levels of lithium in the serum. These include diuretics (e.g., hydrochlorothiazide), nonsteroidal anti-inflammatory agents (e.g., ibuprofen), calcium channel blocking agents (e.g., verapamil), and angiotensin-converting enzyme inhibitors (e.g., captopril).

Thyroid impairments have been observed in individuals receiving lithium therapy, and possible thyroid effects from lithium in drinking water have been reported. Further, there is sufficient evidence available to conclude that therapeutic use of lithium causes developmental effects in offspring when maternal serum lithium concentrations are within the therapeutic range.

ATSDR cannot determine if chronic consumption to 200-500 ug/L of lithium in drinking water represents a public health concern. Note, these levels are unlikely to affect individuals already on lithium therapy as they would be very small (about 1,000 times less) compared to therapeutic doses; furthermore, these individuals should be having lithium levels measured periodically and doses adjusted accordingly.

A Lowest Observable Adverse Effect Level (LOAEL) has not been identified for lithium ingestion. In 2008, EPA developed a conservative provisional reference dose (RfD) for lithium ingestion of 2 ug/kg/day. In the absence of a LOAEL for lithium ingestion, EPA assigned the LOAEL to 2.1 mg/kg/day, which was estimated as the lowest value at which therapeutic effects were recognized, and then applied multiple uncertainty factors. Adverse effects in multiple organ systems have been noted at all therapeutic levels but are generally accepted to be related to increasing therapeutic serum levels. EPA used an uncertainty factor (UF) of 1,000 in this provisional RfD derivation (10 for LOAEL, 10 for human variability, and 10 for database uncertainty). The additional UF of 10 for database sufficiency is generally not used in ATSDR's derivations of health guidance values. Without the extra uncertainty factor of 10, a provisional guide for chronic exposures for a child would be approximately 200 ug/L of lithium in drinking water (i.e., 20 ug/kg/day X 10 kg child / 1 L/day) or 700 ug/L of lithium in drinking water for an adult (i.e., 20 ug/kg/day X 70 kg / 2 L/day). Using EPA's provisional RfD, screening value concentrations in drinking water can be calculated as 70 ug/L (for adults weighing 70 kg drinking 2 L/day), 20 ug/L for a 10 kg infant/child drinking 1 L/day, and 32 ug/L (for a 16 kg child drinking 1 L/day). It is very unlikely that levels of 200-500 ug/L of drinking water would be associated with acute toxicity. There are a few epidemiologic studies associating varying levels of lithium in drinking water with behavioral effects and effects on thyroid functions. There is a wealth of literature on therapeutic use of lithium and adverse effects over time at doses that are much higher than these environmental exposures. Further study would need to be done to fully understand the effect of chronic lithium drinking water exposure at environmental exposures less than therapeutic exposures.

DRO Rep: Dir DRO	Regional Rep: Lora Werner	DRO Concurrence: ✓
DRO Rep Signature:	Regional Rep Signature:	